REMARKS

Claims 1-4, 7, 14 and 23 are currently pending and stand rejected. Claims 7 and 23 are amended and claims 2-4 are cancelled herein. Support for the present claim amendments can be found throughout the specification and claims as originally filed, and as set out below. No new matter is added and entry is respectfully requested.

December 16, 2003 Interview

Applicants greatly appreciate the thoughtful consideration shown their undersigned representative and patent counsel for assignee in an interview on 16 December 2003.

The substance of the interview is hereby made of record as directed by MPEP § 713.04. The interview of 16 December 2003 took place between Examiner Alana M. Harris, Timothy Lithgow of the assignee (Agensys), and the undersigned agent. Written description, enablement and anticipation issues were discussed as they relate to claims 7 and 23. Proposed claim amendments were provided. The general thrust of the principal arguments focused on the written description and enablement rejections; in particular, the functional and structural claim limitations of claims 7 and 23 were discussed, and arguments were presented that 90% identical protein variants of SEQ ID NO:2 (limited to conservative substitutions and wherein the protein is specifically bound by an antibody that specifically binds SEQ ID NO:2) are described and enabled. Agreement was not reached. Examiner Harris indicated that she would consult with Examiner Caputa regarding the outstanding Written Description and Enablement issues as they pertain to the proposed claims.

On December 19, 2003, Examiner Harris called the undersigned and indicated that she had spoken with Examiner Caputa about the proposed claim amendments and another similar claim in another pending (but unrelated) application (U.S. Application No. 09/389,000, currently assigned to Agensys, Inc.) that is currently considered allowable. Further, Examiner Harris invited the undersigned to specifically indicate which claim(s) in U.S. Application No. 09/389,000 are comparable in form to claims 7 and 23 of the present application. Respectfully, claim 68 of U.S. Application No. 09/389,000 is comparable in form (*i.e.*, utilizing conservative substitutions and antibody binding as a function) but not substance to currently amended claims 7 and 23 (see Exhibit A).

Rejections Under 35 U.S.C. § 112, First Paragraph

New Matter Rejection

Claims 7 and 23 stand rejected under 35 U.S.C. § 112, first paragraph, as purportedly failing to comply with the written description requirement. The Office has specifically requested that the Applicants provide the page and line numbers where support for these claims can be found. Accordingly, support for the limitation that "any amino acid substitutions are conservative substitutions" can be found, *inter alia*, at page 19, lines 31-33; page 20, lines 4-19; original claim 7. Support for the limitation to an "isolated 125P5C8 protein that is at least 90% identical to the amino acid sequence of SEQ ID NO: 2 over the entire length of SEQ ID NO: 2," can be found, *inter alia*, at page 9, lines 27-28; page 19, line 30 to page 20, line 2; page 21, lines 12-13; original claim 13. Support for the limitation providing that "the protein is specifically bound by an antibody that specifically binds a 125P5C8 protein having the amino acid sequence of SEQ ID NO: 2" can be found, *inter alia*, at page 6, lines 10-12; page 10, line 34-page 11, line 3; page 12, lines 3-29; page 21, lines 5-7; page 27, lines 16-19; original claims 24-26. Based on the foregoing, the Applicants respectfully request withdrawal of this rejection.

Written Description - Biological Deposit

The Office has again rejected claim 14 under 35 U.S.C. § 112, first paragraph, as purportedly failing to provide an adequate written description and an enabling disclosure "without complete evidence either that the claimed biological materials are known and readily available to the public or . . . of the deposit of the biological materials . . .." Paper No. 22, page 12. The Office appears to be indicating that there is insufficient assurance that the deposit referenced at page 14, lines 7-9 (as amended on 11 July 2003); page 50, lines 11-13 (as amended on 11 July 2003); and page 55, lines 30-31 (as amended on 11 July 2003) of the specification was made under the conditions specified in 37 C.F.R. § 1.801-1.809.

The Applicants include herewith as **Exhibit B**, the American Type Culture Collection (ATCC) deposit receipt received in connection with the deposit of 125P5C8 cDNA on 1 March 2001 with the ATCC as plasmid *Escherichia coli* DH5A 125P5C8PRO. The deposit was assigned Accession No. PTA-3137. Applicants hereby state that 1) all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on the application, and 2) that the deposit will be replaced if viable samples cannot be dispensed. Applicants reserve the right to

request notice by the depository to the depositor of the name and address of the party to whom a deposit is furnished, as permitted by 37 C.F.R. § 1.808(a)(2) and 37 C.F.R. § 1.808(b).

In light of the foregoing and the previous assurances provided by the undersigned, the Applicants respectfully request withdrawal of this rejection.

Written Description Rejection

The Office has further rejected claims 1-4, 7, 14 and 23 under 35 U.S.C. § 112, first paragraph, as purportedly containing subject matter that was not supported by an adequate written description. The Office has specifically indicated that "Applicants only had possession of SEQ ID NO:2 and not polypeptides that share less than 100% sequence identity with SEQ ID NO:2." Paper No. 22, page 7. And, that "[t]he specification does not evidence possession of all the possible mutant polypeptides that could be capable [of] exhibiting the alleged wild type 125P5C8 properties . . . , such as a diagnostic marker." *Id.*

"The written description requirement does not require the applicant to describe exactly the subject matter claimed, instead the description must clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1321 (Fed. Cir. 2003) (citation omitted). As such, the original disclosure need not provide *in haec verba* support for the claimed subject matter. *See Fujikawa v. Wattanasin*, 39 USPQ2d 1895, 1904 (Fed. Cir. 1996). Thus, one of skill in the art must be able to recognize that the Applicants demonstrated possession of the claimed invention. Respectfully, the Examples, methods and materials provided in the specification provide such a description for the claimed subject matter. *See, e.g.*, page 6, lines 10-12; page 9, lines 27-28; page 10, line 34-page 11, line 3; page 12, lines 3-29; page 19, line 30 to page 20, line 2; page 20, lines 4-19; page 21, lines 5-7, 12-13; page 27, lines 16-19; original claims 7, 13, 24-26.

With specific regard to the Federal Circuit decision in *The Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) (*Lilly*), in *Moba* (cited above) the Federal Circuit has recently indicated that "the *Lilly* disclosure rule does not require a particular form of disclosure because one of skill in the art could determine from the specification that the inventor possessed the invention at the time of filing." *Moba, B.V.*, 325 F.3d 2d at 1321 (providing also that "the erroneous written description requirement of *Lilly* case lacks both a statutory and a logical foundation" *Id.* at 1323 (Rader, R., concurring)). As further indicated by the Federal

Circuit, "*Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen Inc v. Hoechst Marion Roussel, Inc.*, 65 USPQ2d 1385, 1398 (Fed. Cir. 2003). Based on the foregoing, the Applicants assert herein that adequate structural/functional description is provided.

It is true that Applicants have not tested each and every 125P5C8 variant encompassed in the claims. But clearly, that cannot be the test for "possession"; for that would amount to a requirement of actual reduction to practice to satisfy the "written description" requirement, which is unpermissible under the established legal precedents. *See, e.g., Gould v. Quigg*, 3 U.S.P.Q.2d 1302, 1304 (Fed. Cir. 1987) (an applicant need not have actually reduced the invention to practice prior to filing). As acknowledged by the Office, the Applicants have clearly demonstrated possession of SEQ ID NO:2. The Applicants also presently set forth claims that limit the claimed protein in terms of the type of substitutions (conservative, which are spelled out in the specification) that are permissible within the 90% identical variants, and that an antibody that specifically binds SEQ ID NO:2 must also specifically bind the 90% identical variants. The Applicants assert that one of skill in the art would recognize that these presently claimed variants are supported by the present disclosure. Moreover, the present claims account for the possibility that similar proteins (to SEQ ID NO:2) containing allelic variations, for example, may exist.

As for whether the claim limitations that require an antibody that specifically binds SEQ ID NO:2 also specifically binds the claimed 90% identical (conservative substitution) 125P5C8 proteins provide sufficient functional description of the claimed proteins, the Applicants cite an example where such language has recently been considered allowable. *See, e.g.*, U.S. Application No. 09/389,000 allowed claim 68 (attached hereto as exhibit A). Understandably, descriptive support is fact specific so the Applicants merely reference this case as an example similar to the Examples set out in the Written Description Guidelines. *See* 66 Fed. Reg. 1099 (2001) ("the Guidelines"). As the Guidelines are illustrative of the numerous potential written description issues encountered by the Office, they cannot be considered to comprehensively illustrate the wide variety of practical situations. Numerous variations of the Examples set out in the Guidelines surely exist. Accordingly, the presently amended claims are considered to be supported by a sufficient written

description such that one of skill in the art would recognize that the Applicants had possession of the claimed 90% identical variants of SEQ ID NO:2.

Enablement Rejections

The Office has further rejected claims 1-4, 7, 14 and 23 under 35 U.S.C. § 112, first paragraph, as purportedly not enabled. The Office has specifically indicated that the specification has not set forth sufficient information to make and use the claimed proteins. Moreover, the Office has indicated a concern regarding whether 90% identical conservative substitution variants maintain the same intrinsic activity as the native 125P5C8 protein (as provided, for example, in Example 2, page 55, lines 23-29).

"The enablement requirement is often more indulgent than the written description requirement. The specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation.'" *Amgen v. Hoechst Marion Roussel*, 65 USPQ2d 1385, 1400 (Fed. Cir. 2003) (internal citations omitted).

The Applicants assert that given the present guidance provided in the specification and the limitations set out in the claims, one of skill in the art would understand how to make the subject matter of the present claims. The Office has acknowledged that the Applicants have referenced art accepted means for producing the claimed modifications to SEQ ID NO:2. *See* Paper No. 2, page 9. SEQ ID NO:2 is also specifically provided. Moreover, conservative substitutions are set out, for example, at page 20, lines 4-16 of the specification. And, as indicated in the specification, "[c]onservative amino acid substitutions can frequently be made in a protein without altering either the conformation or function of the protein." *Id.* at lines 4-5.

As for whether the 90% identical 125P5C8 conservative substitution variants maintain "functions that are commensurate with the functions of the native protein"; means are provided in the specification such that these determinations would not involve undue experimentation. *See, e.g.*, pages 19-21; Examples 2-3, 9-10, 12-15. The presently claimed 125P5C8 protein variants are intended to encompass a set that maintains similar activities to that of the native protein and (as indicated) account for the possibility that similar proteins (to SEQ ID NO:2) containing allelic variations, for example, may exist.

The Office further asserts that single amino acid substitutions/alterations can affect the biological activity of the protein. In response, as routine experimentation would confirm, the Applicants assert that given the limitations of the present claims and the supporting description, a variant having a significant alteration in the intrinsic activity of the variant versus of the native protein due to an amino acid substitution/alteration will generally fall outside of the scope of the present claims. It is highly likely that such a variant will not be specifically bound by an antibody that also specifically binds SEQ ID NO:2. Moreover, the conservative substitution limitation is intended to allow for allelic variations, while preserving the activity of the protein.

Rejections Under 35 U.S.C. § 102(a)

Claims 2-4, 7, 14 and 23 stand rejected under 35 U.S.C. § 102(a) as purportedly anticipated by Accession number AK025164.

Claims 2-4 are cancelled herein, thus rendering moot this rejection as it applies to these claims.

Claims 7 and 23 are currently directed to a 125P5C8 protein which is at least 90% identical to the amino acid sequence of SEQ ID NO: 2 over the entire length of SEQ ID NO: 2, wherein any amino acid substitutions are conservative substitutions. Thus, the range or variants encompassed within these claims is limited by the fact that any substitutions are conservative ones. Conservative substitutions are set out in the specification at page 20, lines 4-19.

The alignment provided by the Office between AK025164 and SEQ ID NO: 2 indicates at least one mismatch at amino acid position 689 of SEQ ID NO: 2 (corresponding to nucleotides 2247-2249 of AK025164 in the provided alignment). At positions 2247-2249 of AK025164, the nucleotides "AAT" (adenine-adenine-thymine) are set out. "AAT" encodes the amino acid asparagine; SEQ ID NO: 2, however, lists histidine at this position. Accordingly, the question becomes whether asparagine represents a conservative substitution for histidine. Based on the present disclosure, the Applicants assert that it is not. At page 20 of the present disclosure no conservative substitution is set out for histidine. However, page 20 does provide that the conservative substitution for asparagine is glutamine, and vice versa. Thus, in accordance with the support provided in the specification, AK025164 does not anticipate the present claims as it contains at least one non-conservative amino acid substitution.

Claim 14 is directed to a protein having an Amino acid sequence that is exactly that of SEQ ID NO:2. SEQ ID NO: 1 encodes a protein that is exactly the amino acid sequence of SEQ ID NO:2. The cDNA contained in the plasmid designated *Escherichia coli* DH5A 125P5C8PRO also corresponds to to SEQ ID NO:2. Thus, AK025164 does not disclose a protein that has an amino acid sequence which is exactly that of an amino acid sequence encoded by the polynucleotides of claim 14 As indicated above, AK025164 contains at least one non-conservative amino acid substitution versus SEQ ID NO:2 and accordingly does not anticipate claim 14.

Based on the foregoing, the Applicants respectfully request withdrawal of this rejection of the pending claims.

Claims 2-4, 7, 14 and 23 stand rejected under 35 U.S.C. § 102(a) as purportedly anticipated by Accession number Q9H720, as evidenced by Accession number AK025164.

Claims 2-4 are cancelled herein, thus rendering moot this rejection as it applies to these claims.

With respect to claims 7, 14 and 23, the Applicants respectfully direct the Office's attention to the arguments set forth above pertaining to AK025164. The polypeptide encoded by Q9H720 contains non-conservative substitutions versus the currently claimed proteins and thus does not anticipate the subject matter of present claims 7, 14 and 23. Moreover, with respect to claim 23, this claim contains product by process limitations not present in Q9H720. For example, Q9H720 does not disclose a polynucleotide having the sequence of SEQ ID NO:1, rather, several differences are present. The following mismatches are present:

SEQ ID NO: 1 (position number and nucleotide)	**Corresponding position in Q9H720 (position number and nucleotide)**
339-Guanine	521-Adenine
1119-Cytosine	1301-Thymine
2065-Cytosine	2247-Adenine

Accordingly, Q9H720 does not disclose a polynucleotide having the sequence as shown in Figure 2 (SEQ ID NO:1) from nucleotide residue 1 through nucleotide residue number 2103; or a polynucleotide having the sequence as shown in Figure 2 (SEQ ID NO: 1), from nucleotide residue number 1 through nucleotide residue number 2100; or a polynucleotide having the sequence as shown in Figure 2 (SEQ ID NO: 1), from nucleotide residue number 1 through nucleotide residue number 2097; or a polynucleotide of at least 10 bases of Figure 2 (SEQ ID NO: 1) that comprises

the base at position 339; or a polynucleotide of at least 10 bases of Figure 2 (SEQ ID NO: 1) that comprises the base at position 1119; or a polynucleotide of at least 10 bases of Figure 2 (SEQ ID NO: 1) that comprises the base at position 2065. Thus, both the polynucleotide and the resultant protein differ from the limitations set out in the present claims. Accordingly, the Applicants respectfully request withdrawal of this rejection as it applies to the pending claims.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 511582003500. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: February 9, 2004

Respectfully submitted,

By _____

David L. Devernoe
Registration No.: 50,128
MORRISON & FOERSTER LLP
3811 Valley Centre Drive, Suite 500
San Diego, California 92130
(858) 720-7943